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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/943,687	08/31/2001	Kamel F. Egbaria	MGP-104US	1264

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/943,687	EGBARIA ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF REMARKS, DECLARATION AND THE STATUSOF THE CLAIMS

1. The remarks/arguments and the declaration under Rule 132 filed 2/5/04 are acknowledged, entered and considered. Claims 1-30 are now pending in the application. It is noted that Applicant has not amended the claims and has not argued the rejection under 35 U.S.C. 103(a) over the prior art of record, except for the secondary reference of Li et al. (S.T.P. Pharma Sciences, Vol. 10, No. 4, pp. 341-344, 2000). Applicant has submitted a declaration under Rule 132 and argued that Y, Li (co-author of the publication) is a student and not co-inventor of the instant application and cites *In re Katz*, 687 F. 2d 450, 215 USPQ 14 (CCPA 1982) and concludes by stating that the reference of Li et al., which was relied upon to reject claims 1-30 is shown by this filing not to be prior art, and as such, the rejection has been overcome is unpersuasive. Contrary to Applicant's arguments, the declaration under Rule 132 would not overcome the reference of Li et al. under 35 U.S.C. 102(a) because the activity by another before invention by Applicant is applicable here. For Applicant to overcome the printed publication of Li et al., Applicant has to provide a declaration under Rule 131 to show that the reference describes Applicants work since one of the co-inventor Dr. Kamel Egbaria was not cited in the printed publication. Thus, the rejection under 35 U.S.C. 103 (a) as being unpatentable over Cho et al., (U.S. Patent No. 5,962,019) taken with Li et al. (S.T.P. Pharma Sciences, Vol. 10, No. 4, pp. 341-344, 200) or Kovacs et al., (U.S. Patent No. 5,583,105) is maintained for the reasons of record until Applicant

provides Rule 131 declaration. Further, even if the Li et al. reference is removed, the reference of Li et al. was applied to show the teachings of the formulation of spontaneous emulsion with the diameter of the particles of said spontaneous emulsion as claimed in claims 16, 17 and 28-30. The exclusion of this reference (i.e., Li et al.) would have overcome only the above claims (i.e., claims 16, 17 and 28-30) and not claims 1-30 as argued by Applicant. However, a new reference (i.e., Charman et al., Pharmaceutical Research, Vol. 9, No. 1, pp. 87-93, 1992) is applied to address the limitations of claims 16, 17 and 28-30 in combination with the prior art of record, and since Applicant has not argued with respect to 103(a) rejection over the prior art of record (i.e., Cho et al. and Kovacs et al.), the previous Office action is reiterated and modified with the new reference as they apply to the rejection set forth.

The following is a new ground of rejection.

CLAIMS REJECTION-35 U.S.C. § 103(a)

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were

made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cho et al., (U.S. Patent No. 5,962,019) taken with Charman et al., (Pharmaceutical Research, Vol. 9, No. 1, pp. 87-93, 1992) and Kovacs et al., (U.S. Patent No. 5,583,105).

Cho et al., teach an orally administered pharmaceutical composition comprising cyclosporin (including cyclosporin A), ethanol, polyoxyethtylene compounds and polyoxyethylene derivatives of fatty acids (which includes polyoxyethylene glycerol trioleate), and an oil component (such as ethyl oleate) and a method of preparing such pharmaceutical formulation thereof. The reference discloses various concentrations for oral cyclosporin formulation, wherein the preferred concentration for cyclosporin A ranges from 50 to 150 mg/ml, for alkanols such as ethanol ranges from 5 to 60% (v/v), for oil component such as ethyl oleate ranges from 15 to 75% (v/v), and for polyoxyethylene compounds or derivatives thereof ranges from 5 to 60% (v/v). (See cols. 3-7 and the claims) as directed to claims 1-13 and 18-26.

The reference of Cho et al. differs from claims 1-30 in not teaching the formulation of spontaneous emulsion with the diameter of the particles of said spontaneous emulsion and the specific concentrations and ratios recited in the claims. As acknowledged in the instant specification on page 2, lines 3-15, cyclosporin is highly lipophilic and hydrophobic, and as such sparingly soluble in water and well dissolved in organic solvents. However, the secondary reference of Charman et al., discloses a

formulation of a lipophilic compound, WIN 54954, in a medium chain triglyceride oil/nonionic surfactant mixture, which exhibited self-emulsification under conditions of gentle agitation in an aqueous medium. The resulting oil/water emulsion produced spontaneously because self-emulsifying drug delivery systems (SEDDS) are thermodynamically stable, as opposed to the regular emulsion, which are thermodynamically unstable. The resulting formulation produced dispersion with mean droplet diameters of less than 3 μm, which is about 3000 nm because 1 μm = 1000 nm. Thus, having a diameter of less than 3 μm (i.e., 3000 nm) would include the recited diameter ranges 50 to 185 nm of claims 17 and 28, and 50 to 150 nm of claims 29 and 30 (See e.g., pages 87-88 and 92) as directed to claims 16, 17 and 28-30. Furthermore, as acknowledged on page 2, lines 16 to page 4, lines 21 and Table 1 in the instant specification, such formulation of emulsion or microemulsion are commercially available under tradenames "Neoral" and "SangCya" comprising a formulation of cyclosporin, surfactant such as Tween 80, ethanol and glycerol having a diameter of 30-50 nm (Neoral) and 200-300nm (SangCya). Thus, clearly showing that self-emulsifying drug deliver systems (SEDDS) are a convenient method of delivering hydrophobic drugs with a formulation of a spontaneous emulsion having specific diameter.

With respect to the selection of specific concentrations and ratios as recited in the claims, although, all the references show the ranges claimed, however, Kovacs et al., discloses the specific and preferred concentration ranges and ratios as claimed in the instant invention (See e.g., cols. 1-4 and claims 1 and 8-12) as directed to claims 1-15 and 18-27. Thus, the ranges disclosed in the prior art and claimed by Applicant overlap in scope, and as such, the selection of the appropriate concentrations, diameters, and ratios would have been *prima facie* obvious because where the general

conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation, *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1995).

Therefore, in view of the above and in view of the combined teachings of the prior art makes obvious the claimed invention's orally administered pharmaceutical composition in a form of a spontaneous emulsion comprising cyclosporin (cyclosporin A), ethanol, polyoxyethylene glycerol trioleate, and an oil component (ethyl oleate) and a method of preparing such pharmaceutical formulation thereof, absent of objective factual evidence or unexpected results to the contrary..

CONCLUSION AND FUTURE CORRESPONDENCE

3. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

AAMohamed/AAM

April 15, 2004

Christopher S. F. Low

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SUPERVISORY PATENT EXAMINER
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